

REMARKS

Claims 1-15 were previously cancelled. New Claims 31-33 are presently cancelled as being directed to a non-elected invention. Accordingly, Claims 24-30 are pending.

Present Invention

The present invention provides a novel method for labelling bio-organic molecules. The method allows for a greater number of distinct labels to be generated from a fixed number of stains, paints or dyes, *e.g.*, fluorophores, than have been generated from prior art methods.

In the present specification, the term "colour" is not used in the conventional sense. That is, the term "colour" is not used merely to mean a monochromatic pigment.

Instead, the term "colour" is used to mean a distinct label. Labels may be distinct from one another due to the presence of different mixtures of monochromatic pigments. For example, such pigments may result from the mixing together of different stains, paints or dyes. Additionally, labels may be distinct from one another due to the presence of different monochromatic pigments side by side. Further, labels may be distinct from one another due to the presence of a hapten, or immunogenic/antigenic determinant.

The present method can be used, for example, to selectively label bio-organic molecules, such as chromosomes. Such labelling has many applications, including but not limited to, cytogenetics; cancer research; genomics; proteomics; drug discovery and delivery; and food and feed technology.

Before the present method, selective labelling of chromosomes has typically been accomplished by one of two methods, either binary labelling or ratio labelling.

Binary labelling uses combinations of probes, wherein each individual probe is associated with a distinct label, for example, a distinct fluorophore. Binary labelling is also called combinatorial labelling. Each combination is targeted to a specific bio-organic molecule, for example, a chromosome.

The number of distinct "colours" (n) using k different binary labels is $n=2^k-1$. In the formula, 1 is subtracted from 2^k so as to remove the combination all "colours" are absent.

As can be seen in the table, for example, three fluorophores would generate a maximum of 7 "colours," (*i.e.*, $7=2^3-1$).

	COLOUR						
Fluorophore	1	2	3	4	5	6	7
Blue	+	+	+	-	-	+	-
Red	+	+	-	-	+	-	+
Yellow	+	-	-	+	+	+	-

In the table, a "+" indicates the presence of a fluorophore; and a "-" indicates the absence of a fluorophore.

Thus, five fluorophores would allow a maximum of 31 "colours" ($31=2^5-1$) by binary labelling. Thirty-one "colours" are sufficient to distinctly stain the twenty-four human chromosomes.

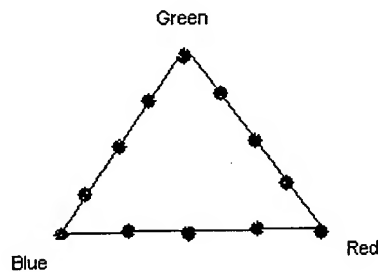
Ratio labelling, by contrast, is based on the *quantity* of each dye present in a mixture of dyes, *i.e.*, signal strength. A certain number of dyes, for example two fluorophores, taken from a pool of spectrally distinct fluorophores, are simultaneously used to produce a certain "colour" taking into account the quantity of each fluorophore. That is, the relative presence (*i.e.*, signal strength) of each fluorophore is assessed.

For example, using a three fluorophore pool, allowing two fluorophores to simultaneously produce a certain "colour," and resolving three distinct ratios for each pair of fluorophores, ratio-labelling provides 12 "colours." The table below provides an illustration.

	COLOUR											
Fluorophore	1	2	3	4	5	6	7	8	9	10	11	12
Green	50	25	75	50	25	75	-	-	-	100	-	-
Red	-	-	-	50	75	25	50	75	25	-	100	-
Blue	50	75	25	-	-	-	50	25	75	-	-	100

As explained above, a "colour" can be viewed as a combined presence of dyes, not necessarily a physical mixture of dyes. Thus, for example, Colour 8 in the table can be viewed as the dual presence of a red fluorophore and a blue fluorophore in a ratio of 75:25, not necessarily as purple. Alternatively, instruments may be set so as to also view the "colour" as a monochromatic mixture of the red and blue fluorophores.

Level 0 of Figure 1 of the application illustrates this table in graphical form. Level 0 of the figure is roughly reproduced below.



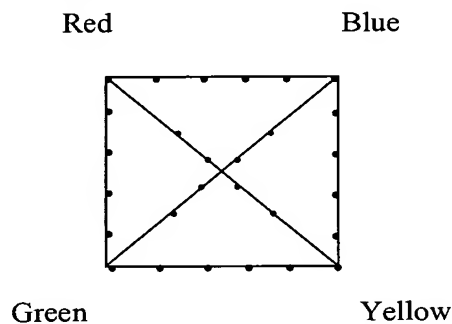
Each dot on the triangle represents a distinct "colour." The dots at each vertex of the triangle represent a "colour" generated solely from a particular fluorophore (Colours 10, 11,

and 12 in the table). The midpoint of each side of the triangle represents a “colour” which is generated from a 50% presence of each of two fluorophores. For example, the midpoint of the left side represents a “colour” which is 50% blue and 50% green (Colour 1 in the table). Moving up one dot represents a “colour” which is 75% green and 25% blue (Colour 3 in the table).

Please note that each side of the triangle has four segments to represent ratios in $\frac{1}{4}$ fractional increments. However, the quantities of two dyes making up a probe may be distinguishable at ratios using lower fractional increments. For example, for ratios using $\frac{1}{5}$ fractional increments, each side of the triangle would be divided into five segments. Ratio labelling is limited by the lowest fractional presence of a dye in a probe, vis-à-vis the other dyes in the same probe, that can be distinctly resolved.

The illustration above is based on a pool of three dyes. A pool of dyes, *i.e.*, a fluorophore pool, may, however, contain more than three dyes.

For example, using a four fluorophore pool, allowing two fluorophores to simultaneously produce a certain “colour,” and resolving four distinct ratios for each pair of fluorophores, ratio-labelling provides 28 “colours.” The square shown below provides an illustration. Each dot represents a “colour.”



Also, more than two dyes can simultaneously be used to produce a certain “colour.” For example, using a three fluorophore pool, all three fluorophores can be used

simultaneously to produce a certain "colour." For example, a green, blue and red fluorophore can each have a 1/3 presence in a certain "colour."

The number of "colours" provided by binary or ratio labelling is insufficient for many applications. As mentioned above, for example, using five dyes, binary labelling provides 31 "colours." Using five dyes, wherein two dyes are used simultaneously to generate each "colour," and distinguishing three ratios, ratio labelling provides 35 "colours." Such a limited number of "colours" provided by these two methods would be insufficient, for example, to distinctly label intrachromosomal rearrangements.

It would thus be necessary to utilize additional dyes to distinctly label such via binary labelling or ratio labelling. The use of additional dyes can be cumbersome, complicated, and expensive. Therefore, the labelling of bio-organic molecules, such as chromosomes, would greatly benefit from a method to increase the number of simultaneously recognizable "colours" producible from a small number of dyes.

The present invention provides a method for generating a greater number of "colours" from a fixed number of different dyes than is generated by the prior art methods. The method constitutes a creative combination of certain elements of binary labelling and of ratio labelling to provide combined binary ratio labelling, *i.e.*, COBRA labelling.

In the COBRA labelling method, a first set of primary probes is labelled via ratio labelling with distinct "colours." This probe set is directed to a first set of targets.

At least one other set of primary probes, directed to a second set of targets, is ratio labelled in exactly the same way as the first primary probe set. However, this second primary probe set additionally contains a binary label, which is spectrally well distinguished from the ratio labels, or contains a biological determinant, *e.g.*, a hapten. This binary label is considered to transform each of the "colours" generated by the ratio labelling of the second

primary probe set into an additional distinct "colour." Thus, the addition of the binary label doubles the number of distinct labels obtained by ratio-labelling.

Figure 1 of the application provides a graphical representation of this concept. A copy is enclosed for the Examiner's convenience. Here, ratio labelling is accomplished by using a three dye pool from which two dyes are used simultaneously to generate each "colour." When no binary label is used (level 0), one set of 12 "colours" is shown to be possible from the three dyes. When one binary label is used (level 1), two sets of 12 "colours" are shown. One set is accompanied by a white rectangle; the second set is accompanied by a red rectangle. The red rectangle represents the binary label. The white rectangle represents the absence of a binary label. Thus, the binary label doubles the number of "colours" provided by the three dyes. Keep in mind that a "colour" as defined in the specification is simply a distinct label.

When two binary labels are used (level 2 in Figure 1), four sets of the 12 "colours," *i.e.*, 48 "colours," are generated. Thus, with the addition of each binary label, the number of "colours" producible from a fixed number of dyes doubles.

As shown in the specification on page 12, lines 29-33, when using only two dyes simultaneously per "colour," the total number of achievable COBRA "colours" (I) can mathematically be described as:

$$I = (n + ((r \times n!) / (2 \times (n - 2)!))) \times 2^m$$

wherein n is the number of dyes used for ratio labelling, m is the number of labels used for binary labelling, and r is the number of ratios that is resolved by ratio labelling; and wherein

$$2 \leq n \leq \infty,$$

$$0 \leq r \leq \infty$$

$$0 \leq m \leq \infty.$$

Request for Finality of Office Action to be Withdrawn

A Second Preliminary Amendment was filed in the instant application on August 21, 2002. The first Office Action issued in the application on September 7, 2004. Note that the first Office Action issued over two years after the Second Preliminary Amendment was filed.

Nevertheless, the first Office Action did not take into account the Second Preliminary Amendment. The instant Office Action *does* take into account the Second Preliminary Amendment, and is, therefore, the **first action on the merits**.

Pursuant to the MPEP 706.07(a), a final Office Action can only be issued on “second or any subsequent actions on the merits.” Accordingly, since the instant Office Action is the *first* action on the merits, the finality of the action is improper.

Applicants’ undersigned representative spoke with the Examiner during the week of June 13, 2005 and pointed out that the finality of the Office Action was improper. The Examiner stated that the representative had a “valid point” and suggested that the Applicants make such point in their response.

Accordingly, Applicants request that the finality of the rejections be withdrawn.

Response to Restriction Requirement

The Examiner has imposed an election requirement restricting the claims to three groups, *i.e.*, Group I: Claims 24-30 reciting a method of distinguishing bio-organic molecules; Group II: Claim 31 reciting a method for labelling probes; and Group III: Claims 32-33 reciting a kit for labelling bio-organic molecules.

The Examiner states that since an action on the merits was issued for the originally presented invention, such invention (embodied in Claims 24-30) was constructively elected

(Office Action, page 4, paragraph 8).

As discussed above, the instant Office Action is the not a proper first action on the merits. However, Applicants have elected Group I, and cancelled Claims 31-33.

Information Disclosure Statement

Applicants had filed an Information Disclosure Statement (IDS) on April 4, 2002 citing five references. The PTO PAIR system indicates that this IDS was received by the PTO on April 15, 2002.

However, the Examiner has not issued an initialed form PTO-1449 by which to acknowledge consideration of the references filed with the IDS. Applicants request consideration of the references cited in the April 4, 2002 IDS, and issuance of a duly initialed form PTO-1449 to evince such consideration. A copy of the April 4, 2002 IDS and form PTO-1449 are enclosed for the Examiner's convenience.

Oath/Declaration

In paragraph 9 of the Office Action, the Examiner states that:

As a result of amendment(s) to the claim(s), the pending claim(s) no longer substantially embrace the invention as set forth in the statement of the invention and/or in the original claim(s). Accordingly, applicant [*sic*] is required to file a supplemental oath or declaration in response to this Office Action.

Applicants do not understand the Examiner's objection. The pending claims relate to a method for distinguishing bio-organic molecules using the COBRA method of labelling. Claims 13-16, as originally filed, also related to the COBRA method of labelling bio-organic molecules. Accordingly, the Applicants request withdrawal of this objection.

Amendments to the Specification

The Examiner alleges that the “title of the invention is not descriptive” (Office Action page 5, paragraph 10). Accordingly, the title of the application has been amended to be “Methods of Labelling Bio-Organic Molecules.”

The Examiner requests that the “use of the trademarks TWEEN 20, NYLON, CYTOCELL, FLUORESCEIN, CHROMA TECHNOLOGY CORP, and LECIA...should be capitalized wherever they appear and be accompanied by generic terminology” (Office Action page 5, paragraph 11). Applicants have made the requested amendments for TWEEN 20TM, CYTOCELL®, CHROMA TECHNOLOGY CORP.®, and LECIA®. However, NYLON and FLUORESCEIN are not trademarks, and thus were not amended.

Additionally, the terms VECTASHIELD®, CYTOVISION®, PENTIUM® and CITIFLUORTM were also amended to indicate their statuses as trademarks.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner rejected Claims 24-30 as failing to comply with the written description requirement (Office Action, paragraphs 14-19). In particular, the Examiner states that the phrase “bio-organic molecules” does not appear in the specification, and thus is new matter.

As stated on page 11, lines 10-17, COBRA can be used for labelling and/or detecting “bio-organic molecules.” The phrase “bio-organic molecules” is clearly defined on page 11, lines 22-24, and recited in Claim 27. In particular, examples of bio-organic molecules are recited as being “nucleic acid, protein, lipid and/or carbohydrate.”

The examples in the specification demonstrate COBRA used to label specific bio-organic molecules. In particular, Examples 13 and 14 (pages 37-45) demonstrate the labelling of chromosomes. Example 15 (pages 45-47) demonstrates COBRA used to label

proteins.

The written description requirement for a claim drawn to a genus is set forth in M.P.E.P §2163 (II)(3)(ii) as follows:

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice....A "representative number of species" means that the species which are adequately described are representative of the entire species...What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed.

Accordingly, Applicants are not required to describe all species within the genus of bio-organic molecules to satisfy the written description requirement. Instead, Applicants are required to provide a representative number of species.

The instant specification sufficiently defines bio-organic molecules and gives a representative number of species. Additionally, two species are specifically exemplified. Accordingly, the written description requirement is satisfied.

Moreover, "there may be situations where one species adequately supports a genus. See, e.g., *In re Rasmussen*, 650 F.2d 1212, 1214, 211 USPQ 323, 326-27 (CCPA 1981)." (See MPEP §2163.05. Emphasis added.) According to the M.P.E.P., in *In re Rasmussen*, a disclosure of even a single method of adheringly applying one layer to another was sufficient to support a generic claim to "adheringly applying" because one skilled in the art reading the specification would understand that it is unimportant how the layers are adhered, so long as they are adhered.

Analogous to *In re Rasmussen*, one skilled in the art reading the instant specification would understand that the type of bio-organic molecule to which the COBRA labelling

method is applied is unimportant. In fact, the specification clearly states on page 47, lines 24-26, that the principle of COBRA labelling is independent of the type of bio-organic molecule targeted. A skilled artisan could predict the operability of the COBRA labelling method to any species other than the ones disclosed.

Furthermore, according to the M.P.E.P. §2163(II)(A)(3)(a) what is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. The description need only describe in detail that which is new or not conventional. (*Hybritech Inc. v. Monoclonal Antibodies, Inc.* 802 F.2d at 1384, 231 USPQ at 94.)

Clearly, a skilled artisan would understand the meaning of “bio-organic molecules,” particularly with the general and specific examples provided in the specification. Such knowledge is well known in the art.

Accordingly, Applicants request that this rejection be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner rejected Claims 24-30 as not being enabled. In particular, the Examiner states that “[w]hile the specification does comprise some examples, said examples are not directed to the general detection of any and all manner of bio-organic molecules under virtually any condition.” (Office Action, paragraphs 20-22)

According to M.P.E.P. § 2164.01, “The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.” Some of the factors considered to determine whether experimentation is undue include the level of one of ordinary skill, the level of predictability in the art, and the existence of working examples (hereinafter referred to as “the *Wands* factors”). (*In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1998).) (See M.P.E.P. § 2164.01(a).)

The instant invention is a method of labelling bio-organic molecules, termed COBRA. As stated on page 47, lines 24-26, of the specification, **the principle of COBRA labelling is independent of the type of bio-organic molecule targeted.** That is, any bio-organic molecules can be labelled by the COBRA labelling method.

All bio-organic molecules are labelled in the same manner. For example, labelling a nucleic acid molecule is done in the same manner as labelling a protein. Labelling molecules is routine in the art. That is, **the level of ordinary skill in the art would include the knowledge of labelling virtually any type of bio-organic molecule.** Accordingly, one of the *Wands* factors has been satisfied.

Also, the instant invention satisfies the *Wands* factor regarding the level of predictability in the art. "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art...The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification." (See M.P.E.P. §2164.03.) As stated above, knowledge of the different types of bio-organic molecules is known in the art, and methods of labelling bio-organic molecules are routine. **It is predictable that if the COBRA labelling method is applicable to the working examples disclosed in the specification, it would be applicable to other bio-organic molecules.**

Additionally, the specification provides **representative examples of bio-organic** molecules, *i.e.*, nucleic acid, protein, lipid and/or carbohydrate; and also provides two specific working examples, *i.e.*, the labelling of chromosomes and the labelling of proteins. Accordingly, a third *Wands* factor has been satisfied.

Moreover, "[f]or a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art would

expect the claimed genus could be used in that manner without undue experimentation.” (See M.P.E.P. §2164.02.) Clearly, Applicants have provided representative examples of bio-organic molecules and have stated that the COBRA method of labelling would apply to the whole genus of bio-organic molecules.

Once the Applicants have met such a standard, according to the M.P.E.P., “[p]roof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced by the examiner to establish that a person skilled in the art could not use the genus as a whole without undue experimentation.” (See M.P.E.P. §2164.02.) The Examiner has not provided adequate reasons to establish that a person skilled in the art could not use the genus as a whole without undue experimentation.

Furthermore, according to the M.P.E.P. §2164.01, “a patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991).” Thus, including a laundry list in the specification of all possible bio-organic molecules, and the routine manners by which to label them, would not only have been unnecessary, but would have been undesirable.

Accordingly, the invention has been sufficiently enabled, and Applicants request that this rejection be withdrawn.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejected Claims 24-30 as being indefinite for the phrases “bio-organic molecule” and “primary labels.” (Office Action, paragraphs 25 and 26, respectively).

According to M.P.E.P. §2173.05(a), “[t]he meaning of every term used in a claim should be apparent from the prior art or from the specification and drawings at the time the application is filed.”

The meaning of “bio-organic molecules” is well known in the prior art. Moreover, the examples of “bio-organic molecules” are given on page 11, lines 22-24, and recited in Claim 27. Accordingly, the meaning of the phrase “bio-organic molecules” is definite. Thus, the metes and bounds of the claims can be easily ascertained.

The phrase “primary label” is defined throughout the specification, including for example, on page 11, lines 24-31. There, each probe in a first probe set is said to be distinctly labelled with a primary label. Primary labels are said to be distinct from one another due to the presence of dyes in distinct ratios, *i.e.*, due to ratio-labelling.

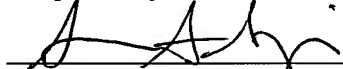
Additionally, a clear illustration of the meaning of “primary labels” is given in Figure 1. Each distinctly colored dot in a triangle represents a “primary label.” Accordingly, Figure 1, Level 0, shows a first set of twelve distinct “primary labels.” Figure 1, Level 1, shows two sets of twelve “primary labels.” Each set is the same as the first set. Figure 1, Level 2, shows four sets of twelve “primary labels.” Each set is the same as the first set.

Accordingly, the meaning of the phrase “primary labels” is definite. Thus, the metes and bounds of the claims can be easily ascertained.

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Applicants respectfully submit that the application is in proper form for allowance which action is earnestly solicited. If resolution of any remaining issue is required prior to allowance of the application, it is respectfully requested that the examiner contact applicant's undersigned attorney at the telephone number provided below.

Respectfully submitted,



Susan A. Sipos, Esq.
Registration No.: 43,128
Attorney for Applicant

HOFFMANN & BARON, LLP
6900 Jericho Turnpike
Syosset, New York 11791
(516) 822-3550
SAS

207051



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Herman Volkers, et al.

Examiner: Unassigned

Serial No.: 10/005,371

Group Art Unit: Unassigned

Filed: December 5, 2001

Docket: 570-21 CPA/CON

For: APPLICATIONS WITH AND
METHODS FOR PRODUCING
SELECTED INTERSTRAND CROSS-
LINKS IN NUCLEIC ACIDS

Dated: April 4, 2002

I hereby certify this correspondence is being deposited
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Assistant Commissioner for Patents
Washington, D.C. 20231

on April 4, 2002
Signature: [Handwritten Signature]

INFORMATION DISCLOSURE STATEMENT

Sir:

In order to fulfill the requirements of candor and good faith set forth in 37 C.F.R.

§1.56, Applicants submit herewith the following Information Disclosure Statement in
accordance with the provisions of 37 C.F.R. §1.97 and §1.98.

ARTICLES

1. Lichter, Peter, "Multicolor FISHing: What's the catch?," TIG, December 1997,
Vol. 13. No.12, pp. 475-479.

2. Lengauer, Christoph, et al., "Chromosomal bar codes produced by multicolor
fluorescence *in situ* hybridization with multiple YAC clones and whole chromosome painting
probes," Human Molecular Genetics, 1993, Vol. 2., No.5, pp. 505-512.

3. Wiegant, J., et al., "Multiple and sensitive fluorescence *in situ* hybridization
with rhodamine-, fluorescein-, and coumarin-labeled DNAs," Cytogenetics and Cell
Genetics, 63:73-76, 1993, pp. 47-51.

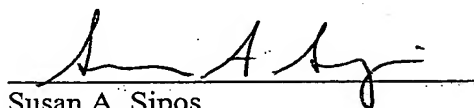
4. Ried, Thomas, et al., "Simultaneous visualization of seven different DNA probes by *in situ* hybridization using combinatorial fluorescence and digital imaging microscopy," Proc. Natl. Acad. Sci, U.S.A., February 1992, Vol. 89, pp. 1388-1392.

5. Dauwerse, J.G., et al., "Multiple colors by fluorescence *in situ* hybridization using ratio-labelled DNA probes create a molecular karyotype," Human Molecular Genetics, Vol. 1, No. 8, pp. 593-598.

A separate listing of all the references has been set forth on the accompanying form PTO-1449. The Examiner is respectfully requested to consider these references in their entirety, and to indicate that he has done so by initialing the form PTO 1449.

If the Examiner has any questions or comments relating to the present application, he or she is respectfully invited to contact Applicants' attorney at the telephone number set forth below.

Respectfully submitted,



Susan A. Sipos
Registration No.: 43,128
Attorney for Applicants

HOFFMANN & BARON, LLP
6900 Jericho Turnpike
Syosset, New York 11791
(516) 822-3550
SAS/jjc



FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE (Rev. 2-32) PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)	ATTY. DOCKET NO. 570-21 CPA/CON	SERIAL NO. 10/005,371
	APPLICANT Volkers, et al.	CONFIRMATION NO.
	FILING DATE December 5, 2001	GROUP Unassigned

U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUB CLASS	FILING DATE IF APPROPRIATE

FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB CLASS	TRANSLATION	
						YES	NO

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

			Lichter, Peter, "Multicolor FISHing: What's the catch?," TIG, December 1997, Vol. 13. No.12, pp. 475-479.
			Lengauer, Christoph, et al., "Chromosomal bar codes produced by multicolor fluorescence <i>in situ</i> hybridization with multiple YAC clones and whole chromosome painting probes," Human Molecular Genetics, 1993, Vol. 2., No.5, pp. 505-512.
			Wiegant, J., et al., "Multiple and sensitive fluorescence <i>in situ</i> hybridization with rhodamine-, fluorescein-, and coumarin-labeled DNAs," Cytogenetics and Cell Genetics, 63:73-76, 1993, pp. 47-51.
			Ried, Thomas, et al., "Simultaneous visualization of seven different DNA probes by <i>in situ</i> hybridization using combinatorial fluorescence and digital imaging microscopy," Proc. Natl. Acad. Sci, U.S.A., February 1992, Vol. 89, pp. 1388-1392.
			Dauwerse, J.G., et al., "Multiple colors by fluorescence <i>in situ</i> hybridization using ratio-labelled DNA probes create a molecular karyotype," Human Molecular Genetics, Vol. 1, No. 8, pp. 593-598.

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication with applicant.